

A Multi-Institutional Evaluation of Antibody-Mediated Rejection Utilizing the PHTS Database: Incidence, Therapies, and Outcomes

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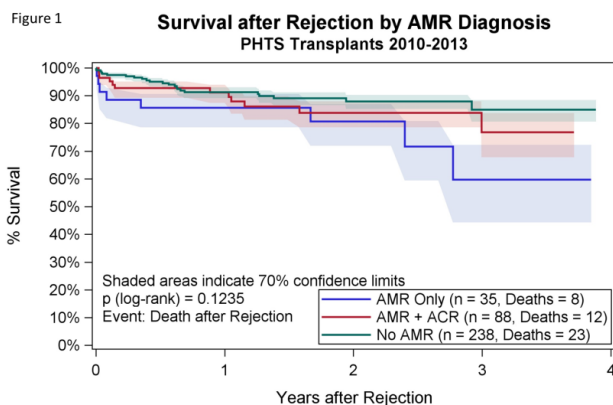
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Introduction: Current knowledge of antibody-mediated rejection (AMR) after heart transplantation (HT) stems largely from adult data with only a few small single-center pediatric studies. Using the multi-institutional Pediatric Heart Transplant Study (PHTS) database, we aimed to report the incidence of AMR, describe contemporary treatment, and evaluate outcomes for treated AMR in children after HT.

Methods: We queried the PHTS database for patients < 18 yrs undergoing primary HT between 1/10 - 12/13. An AMR episode was defined as either a biopsy (bx) with histology and/or complement staining consistent with pathologic AMR or a rejection event attributed to donor specific antibodies based on immunotherapy augmentation directed against antibody production. Biopsy data, treatment strategies, and survival were analyzed.

Results: AMR was reported in 118/1217 (10%) HT recipients and accounted for 142/467 (30%) rejection episodes. AMR was diagnosed by bx in 108 episodes and by Ab-directed therapy in 27 with negative bx and 7 with no bx performed. 100 episodes had concurrent acute cellular rejection (ACR) by bx. 91% and 89% of patients were free from AMR at 1 and 3 years, respectively. AMR therapies included IVIG (n=81, 57%), plasmapheresis (n=61, 43%), rituximab (n=55, 39%), bortezomib (n=16, 11%), and eculizumab (n=1, 1%). 19 patients (16%) died after developing AMR. Mortality did not differ between the AMR, AMR+ACR, and no AMR groups. (Fig. 1) The 1 and 3 year patient survival after initial AMR diagnosis was 89% and 72%, respectively.



Conclusions: This is the largest multi-institutional assessment to date of AMR in pediatric HT recipients. AMR was common and often occurred concurrently with ACR. This study highlights wide variability in both the diagnosis and treatment of AMR. The outcomes of those with AMR were comparable to those with rejection not due to AMR. Ongoing collaborative studies are needed to better characterize AMR and determine treatment effects specific to pediatric HT.